

and insert the following therefor as a separate page after the claims:

-Abstract of the Disclosure

a¹
Compounds are disclosed having the general formula R_1-X-R_2 , wherein R_1 and R_2 are biologically active groups, at least one of which is polypeptidic. X is a non-peptidic polymeric group. R_1 and R_2 may be the same or different. Preferred R_1 and R_2 groups are TNF inhibitors.

In the Claims

Please delete claims 1-14 and 16-44, without prejudice or disclaimer.

Please amend claim 15, as follows:

a²
15. A [substantially purified] compound of the formula R_1-X-R_2 , wherein:

[X comprises a non-peptidic polymer having a first reactive group and a second reactive group, wherein said first reactive group is a Michael acceptor; and]

R_1 and R_2 are each a tumor necrosis factor (TNF) inhibitor polypeptide selected from:

(a) 30 kDa TNF inhibitor or 40 kDa TNF inhibitor,

(b) 30 kDa TNF inhibitor or 40 kDa TNF inhibitor, modified to contain at least one non-native cysteine residue, and

(c) a biologically active portion of (a) or (b), wherein R_1 and R_2 bind to TNF; and

[comprises a biologically-active molecule having a reactive thiol moiety, said biologically-active molecule is covalently bonded to said non-peptidic polymer by reaction of said thiol moiety with said Michael acceptor, and said biologically-active molecule retains its biological activity after said reaction; and

R_2 comprises a biologically-active molecule or a nonbiologically-active group bonded to said non-peptidic polymer by reaction with said second reactive group]

X is a non-peptidic polymer having two activated groups linked thereto, said non-peptidic polymer being selected from polyethylene glycol, polypropylene glycol, polyoxyethylated glycerol and other polyoxyethylated polyols, polyvinyl alcohol and other polyalkylene oxides, polyoxyethylated sorbitol or polyoxyethylated glucose.

Please add the following new claims:

a³
~~45~~⁴⁶. The compound of claim ~~15~~¹⁶, wherein R_1 and R_2 are identical.

- 3
46. The compound of claim ~~13~~¹, wherein R₁ and R₂ are different.
- 4
47. The compound of claim ~~13~~¹, wherein R₁ and R₂ are said 30 kDa TNF inhibitor.
- 5
48. The compound of claim ~~47~~⁴, wherein said 30 kDa TNF inhibitor is modified to contain at least one non-native cysteine residue.
- 6
49. The compound of claim ~~48~~⁵, wherein said non-native cysteine residue is found at an amino acid residue site selected from the group consisting of 1, 14, 105, 111 and 165.
- 7
50. The compound of claim ~~13~~¹, wherein R₁ and R₂ are each a portion of said 30 kDa TNF inhibitor.
- 8
51. The compound of claim ~~13~~¹, wherein R₁ and R₂ are covalently bonded to X by thio-ether bonds.
- 9
52. The compound of claim ~~51~~¹, wherein cysteine residues of R₁ and R₂ are part of said thio-ether bonds.
- 10
53. The compound of claim ~~13~~¹, wherein R₁ and R₂ are attached to said polyethylene glycol via a cysteine residue.
- 11
54. A pharmaceutical composition comprised of an effective amount of the compound of claim ~~13~~¹ in a pharmacologically acceptable carrier.
- 12
55. The compound of claim ~~13~~¹, which has been prepared by a method comprising simultaneously reacting R₁ and R₂ with X, wherein X has at least two reactive groups capable of forming thio-ether bonds when reacted with cysteine amino acid residues.
- 13
56. The compound of claim ~~55~~¹², wherein R₁ and R₂ are said 30 kDa TNF inhibitor or a portion thereof, modified to contain a non-native cysteine residue.
- 14
57. The compound of claim ~~13~~¹², which has been prepared by a method comprising reacting R₁ with X to form a complex R₁-X and subsequently reacting said complex R₁-X with R₂ to form the compound R₁-X-R₂, wherein X has at least two reactive groups capable of forming thio-ether bonds when reacted with cysteine amino acid residues.
- 15
58. The compound of claim ~~57~~¹⁴, wherein R₁ and R₂ are said 30 kDa TNF inhibitor or a portion thereof, modified to contain a non-native cysteine residue.